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IMMUNEX CORPORATION
LAW DEPARTMENT
1201 AMGEN COURT WEST
SEATTLE, WA 98119

EXAMINER	
GAMETT, DANIEL C	

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Please find below and/or attached an Office communication concerning this application or proceeding.

EXAMINER'S AMENDMENT

Applicant's amendments of 04/28/2005 have been entered in full. Claims 1-80 are cancelled. New Claims 81-117 are pending.

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with David B. Ran on 07/20/2005.

The application has been amended as follows:

In the claims:

81. cancelled

82. (Newly amended) A composition comprising a plurality of isolated antibodies or antigen-binding fragments thereof, wherein each of said antibodies or antigen-binding fragments of said plurality specifically binds to an isolated and purified humanTRAIL-R receptor protein ~~of claim 81~~, wherein said isolated and purified human TRAIL-R receptor protein is a product made by the process comprising the steps of:

(a) isolating plasma membranes from Jurkat cells;

(b) solubilizing and homogenizing said isolated plasma membranes of step (a);

(c) centrifuging said solubilized and homogenized isolated plasma membranes of step (b) to yield a plasma membrane extract and a pellet;

(d) applying said plasma membrane extract of step (c) to an anti-octapeptide monoclonal antibody affinity chromatography column, whereby said column of

step (d) adsorbs non-specifically bound material and wherein said octapeptide has the sequence presented in SEQ ID NO: 5;

(e) applying column flow-through from step (d) to an octapeptide-TRAIL ligand affinity chromatography column, whereby said column of step (e) specifically binds said TRAIL-R receptor protein and wherein said octapeptide—TRAIL ligand is a fusion protein of said octapeptide having the sequence presented in SEQ ID NO:5 and TRAIL ligand;

(f) eluting fractions with TRAIL ligand binding activity from said column of step (e); and,

(g) purifying said fractions of step (f) by reverse-phase HPLC to yield said isolated and purified TRAIL-R receptor protein, wherein said isolated and purified TRAIL-R receptor protein has a molecular weight of about 50 to 55 kilodaltons as determined by SDS polyacrylamide gel electrophoresis, and comprises the amino acid sequence VPANEGD (amino acids 327-333 of SEQ ID NO: 2).

83. (Previously presented) The composition of claim 82, wherein said antibodies or antigen-binding fragments specifically bind to membranes of Jurkat cells.

84. (Newly amended) The composition of claim 83, wherein said antibodies or antigen-binding fragments ~~specifically bind to the extracellular domain of TRAIL-R receptor (TRAIL-R) protein and wherein said antibodies or antigen-binding fragments~~ block binding of TRAIL ligand to said TRAIL-R receptor protein.

85. (Previously presented) The composition claim 82, wherein said antibodies are monoclonal antibodies.

86. (Previously presented) The composition of claim 83, wherein said antibodies are monoclonal antibodies.

87. (Previously presented) The composition of claim 85, wherein said antibodies are humanized.

88. (Previously presented) The composition of claim 86, wherein said antibodies are humanized.

89. (Currently amended) A ~~pharmaceutical~~ composition comprising a composition of claim 82, in a physiologically acceptable excipient, diluent, or carrier.

90. (Currently amended) A ~~pharmaceutical~~ composition comprising a composition of claim 83, ~~in~~ and a physiologically acceptable excipient, diluent, or carrier.

91. (Currently amended) A ~~pharmaceutical~~ composition comprising a composition of claim 85, ~~in~~ and a physiologically acceptable excipient, diluent, or carrier.

92. (Currently amended) A ~~pharmaceutical~~ composition comprising a composition of claim 86, ~~in~~ and a physiologically acceptable excipient, diluent, or carrier.

93. (Currently amended) A ~~pharmaceutical~~ composition comprising a composition of claim 87, ~~in~~ and a physiologically acceptable excipient, diluent, or carrier.

94. (Currently amended) A ~~pharmaceutical~~ composition comprising a composition of claim 88, ~~in~~ and a physiologically acceptable excipient, diluent, or carrier.

95-99. cancelled.

100. (Currently amended) A composition comprising a plurality of isolated monoclonal antibodies or antigen-binding fragments thereof, wherein each of said antibodies or antigen-binding fragments thereof ~~of said plurality~~ specifically bind to a human TRAIL receptor (TRAIL-R) protein, said antibodies made by the process of:

(a) immunizing a mouse with an isolated and purified TRAIL receptor (TRAIL-R) protein ~~of claim 81~~ wherein said isolated and purified human TRAIL-R receptor protein is a product made by the process comprising the steps of:

(*1*) isolating plasma membranes from Jurkat cells;

(*2*) solubilizing and homogenizing said isolated plasma membranes of step (*1*);

(*3*) centrifuging said solubilized and homogenized isolated plasma membranes of step (*2*) to yield a plasma membrane extract and a pellet;

(*4*) applying said plasma membrane extract of step (*3*) to an anti-octapeptide monoclonal antibody affinity chromatography column, whereby said column of step (*4*) adsorbs non-specifically bound material and wherein said octapeptide has the sequence presented in SEQ ID NO: 5;

(*5*) applying column flow-through from step (*4*) to an octapeptide-TRAIL ligand affinity chromatography column, whereby said column of step (*5*) specifically binds said TRAIL-R receptor protein and wherein said octapeptide-TRAIL ligand is a fusion protein of said octapeptide having the sequence presented in SEQ ID NO:5 and TRAIL ligand;

(*6*) eluting fractions with TRAIL ligand binding activity from said column of step (*5*); and,

(*7*) purifying said fractions of step (*6*) by reverse-phase HPLC to yield said isolated and purified TRAIL-R receptor protein, wherein said isolated and purified TRAIL-R receptor protein has a molecular weight of about 50 to 55 kilodaltons as determined by SDS polyacrylamide gel electrophoresis, and comprises the amino acid sequence VPANEGD (amino acids 327-333 of SEQ ID NO: 2);

(b) generating hybridomas by fusing murine myeloma cells with spleen cells obtained from said immunized mouse of step (a);

(c) screening said hybridomas of step (b) for reactivity to purified TRAIL-R receptor protein;

(d) isolating and purifying a plurality of monoclonal antibodies expressed by said hybridomas of step (c), wherein said monoclonal antibodies specifically bind to said TRAIL-R receptor protein.

101. (Currently amended) The composition of claim 100, wherein said monoclonal antibodies are humanized.

102. (Currently amended) A ~~pharmaceutical~~ composition comprising a composition 100, ~~in~~ and a physiologically acceptable excipient, diluent, or carrier.

103. (Currently amended) A ~~pharmaceutical~~ composition comprising a composition 101, ~~in~~ and a physiologically acceptable excipient, diluent, or carrier.

104. cancelled.

105. (Currently amended) ~~A~~ The composition of claim 82, ~~comprising a plurality of isolated antibodies or antigen-binding fragments thereof, wherein each of said antibodies or antigen-binding fragments of said plurality specifically binds to an isolated TRAIL-R protein of claim 104~~, wherein said isolated and purified human TRAIL-R receptor protein further comprises the sequence of SEQ ID NO: 4.

106. (Previously presented) The composition of claim 105, wherein said antibodies or antigen-binding fragments thereof specifically bind to membranes of Jurkat cells, in and wherein said Jurkat cells are expressing TRAIL-R receptor protein.

107. (Currently amended) The composition of claim 106, wherein said antibodies ~~specifically bind to the extracellular domain of TRAIL receptor TRAIL-RI protein and wherein said antibodies~~ block binding of TRAIL ligand to said TRAIL-R receptor protein.

108. (Previously presented) The composition claim 105, wherein said antibodies are monoclonal antibodies.

109. (Previously presented) The composition claim 106, wherein said antibodies are monoclonal antibodies.

110. (Previously presented) The composition of claim 108, wherein said antibodies are humanized.

111. (Previously presented) The composition of claim 109, wherein said antibodies are humanized.

112. (Currently amended) A ~~pharmaceutical~~ composition comprising a composition of claim 105, ~~in~~ and a physiologically acceptable excipient, diluent, or carrier.

113. (Currently amended) A ~~pharmaceutical~~ composition comprising a composition of claim 106, ~~in~~ and a physiologically acceptable excipient, diluent, or carrier.

114. (Currently amended) A ~~pharmaceutical~~ composition comprising a composition of claim 108, ~~in~~ and a physiologically acceptable excipient, diluent, or carrier.

115. (Currently amended) A ~~pharmaceutical~~ composition comprising a composition of claim 109, ~~in~~ and a physiologically acceptable excipient, diluent, or carrier.

116. (Currently amended) A ~~pharmaceutical~~ composition comprising a composition of claim 110, ~~in~~ and a physiologically acceptable excipient, diluent, or carrier.

117. (Currently amended) A ~~pharmaceutical~~ composition comprising a composition of claim 111, ~~in~~ and a physiologically acceptable excipient, diluent, or carrier.

Suspension

Claims 82-94, 100-103 and 105-117 are allowable. However, due to a potential interference, *ex parte* prosecution is SUSPENDED FOR A PERIOD OF 6 MONTHS from the date of this letter. Upon expiration of the period of suspension, applicant should make an inquiry as to the status of the application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel C Gamett, Ph.D., whose telephone number is 571 272 1853. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571 272 0961. The fax phone number for the organization where this application or proceeding is assigned is 571 273 8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DCG
Art Unit 1647
20 July 2005

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600